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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/781,069

02/18/2004

Armin Meinzer

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1856

1095

7590

07/07/2009

NOVARTIS  
CORPORATE INTELLECTUAL PROPERTY  
ONE HEALTH PLAZA 104/3  
EAST HANOVER, NJ 07936-1080

EXAMINER

CHANNAVAJJALA, LAKSHMI SARADA

ART UNIT

PAPER NUMBER

1611

MAIL DATE

DELIVERY MODE

07/07/2009

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/781,069	<b>Applicant(s)</b> MEINZER ET AL.	
	<b>Examiner</b> Lakshmi S. Channavajjala	<b>Art Unit</b> 1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 21 April 2009.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 12-24 and 26 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 12-24 and 26 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

Receipt of amendment and response dated 4-21-09 is acknowledged.

Claims 1-11 and 25 are canceled. Claims 12-24 and 26 are pending.

#### ***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4-21-09 has been entered.

#### ***Terminal Disclaimer***

2. The terminal disclaimer filed on 4-21-09 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of US 6,432,445 and US 6,767,555 has been reviewed and is accepted. The terminal disclaimer has been recorded.

3. The following rejection has been maintained:

#### ***Claim Rejections - 35 USC § 103***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. Claims 12-24 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,342,625 to Hauer et al (Hauer) in view of US 5,962,019 ('019) to Cho.

Hauer teaches cyclosporin comprising pharmaceutical compositions in the form of microemulsion pre-concentrates and that are filled in hard gelatin capsules (abstract, examples, col. 29, lines 11-14). Examples in col. 26-29 are directed cyclosporin formulation, which include surfactants Cremophor RH 40, which is described as a reaction product of hydrogenated or natural vegetable oil and ethylene glycol, with an HLB value of 14-16. Thus, the surfactant of Hauer meets the claimed surfactant component. Hauer also teaches composition comprising propylene glycol and ethanol that read on the claimed lower alkanols (col. 18, last paragraph to col. 19, 1<sup>st</sup> paragraph). The pre-concentrate compositions of Hauer are free of water and form spontaneous emulsions (col. 5, lines 57 through col. 6, lines 35) and hence meet the claims 22, 23 and 26. Hauer teaches various amounts of cyclosporin in the examples that is within the claimed ranges (claim 16). Not all of the compositions of Hauer contain additional oils and therefore read on the less than 5% of oils apart from those present in the surfactant.

Hauer fails to teach polyethylene glycol in combination with the lower alkanols. Cho teaches hard gelating capsules comprising cyclosporin formulations (abstract, col. 3 L 10-25). Cho teaches that the compositions contain an orally acceptable vehicle comprising at least one alkanol solvent constituting an alkanol having 2 to 3 carbon atoms and a co-solvent selected from fatty acids and diols (col. 4, L 28-41). Among the diols, Cho teaches the claimed polyethylene glycols (col. 5, L 1-25 and examples in col. 8-10). 'Cho teach incorporating at least one surfactant, such as polyoxyalkylene surfactant having an HLB value of 5 to 20 or preferably 8 to 16. Thus, both Hauer and

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Cho teaches cyclosporin compositions comprising a surfactant and hydrophilic solvents, constituting analogous art. Therefore, it would have been obvious for one of an ordinary skill in the art at the time of the instant invention to include polyethylene glycol, of Cho in the cyclosporin composition of Hauer as a co-solvent for the lower alkanol solvent of because Cho teaches that the polyethylene glycol co-solvents adsorb water molecules, which may be present in the formulations thereby reducing the possibility for precipitation of the cyclosporin from the formulations, and also impart desirable properties such as viscosity, stability etc. Accordingly, a skilled artisan would have expected to achieve greater stability of the composition of Hauer containing cyclosporin by incorporating the PEG of '019. Further, optimizing the amount of solvents and co-solvents in the composition of Hauer with an expectation to achieve the desired solubility and optimum stability would have been within the scope of a skilled artisan. While Hauer does describe oils, the examples of Hauer do not necessarily contain oils while instant claims recite that less than 5% of oils apart from those present in the surfactant, applicants have not shown any unexpected advantage with the claimed limit of less of than 5%.

### ***Response to Argument***

Applicant's arguments filed 4-21-09 have been fully considered but they are not persuasive.

Applicants argue that Cho teaches at least one non-ionic polyoxyalkylene surfactant such as BRIJ 30 and TWEEN 80, which are not included in the present amended claims. It is argued that why a person of ordinary skill in the art should

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would have chosen to include PEG of Cho but omit the nonionic surfactant of Cho in the instant claims. Applicants' arguments are not persuasive because the teachings of Cho have been cited for including polyethylene glycol, which is absent in Hauer. In response to the argument that examiner failed to address that Cho teaches non-ionic surfactant as an essential element, examiner states that the primary reference of Hauer does not require any nonionic surfactants. MPEP 2145 states that the prior art's mere disclosure of more than one alternative does not constitute a teaching away from any of these alternatives because such disclosure does not criticize, discredit, or otherwise discourage the solution claimed. Further, exemplary rationales that may support a conclusion of obviousness include known work in one field of endeavor may prompt variations of it for use in either the same field or a different one based on design incentives or other market forces, if the variations are predictable to one of ordinary skill in the art. *KSR International v. Teleflex, Inc.*, 82 USPQ 2d 1385 (U.S. 2007). Thus, while a skilled artisan would have understood from the teachings of Hauer that cyclosporine microemulsion concentrate may be prepared with nonionic surfactants, a skilled artisan would also have employed the combination of PEG with lower alkanols of Hauer so as to reduce excess water, suggested by Cho who suggests polyethylene glycol for the advantage of absorbing water molecules that may be present in the composition thereby reducing the possibility for precipitation of the cyclosporine and also impart the desired viscosity and stability.. Thus, a skilled artisan would still have been able to prepare an emulsion concentrate without nonionic surfactants of Cho, in light of the teachings of

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Cho. A skilled artisan preparing microemulsions without or minimum amounts of water would have looked at the teachings of Cho, also directed to cyclosporine compositions where excess water is absorbed to impart stability. In contrast to the argument that the prior art does not provide a motivation to include the non-ionic surfactants of Cho in the composition of Hauer, as explained above, the examiner relied on Cho for PEG and not nonionic surfactants. Further, Cho does not teach any specific advantage of nonionic surfactants or a combination of nonionic surfactants with PEG. Instead, Cho teaches the advantages of the combination of PEG and lower alkanols such as ethanol. Furthermore, while MPEP states that omission of an element and its function is obvious if the function of the element is not desired, applicants merely argue without showing that the unexpected advantage of omitting other components such as nonionic surfactants of Cho.

The following is a new rejection:

4. Claims 12-24 and 26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.
5. A careful review of the instant specification does not support a composition with the instant the transitional phrase "consisting of" a) cyclosporin A, b) a surfactant of HLB value of at least 10 comprising a reaction product of natural or hydrogenated vegetable oil and ethylene glycol, and c) a hydrophilic phase comprising a polyethylene

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glycol and at least one lower alkanol selected from ethanol and propylene glycol. The exemplified compositions do not provide support for the composition consisting of a combination polyethylene glycol and at least one lower alkanol selected from ethanol and propylene glycol, instead supports only PEG alone or either one of propylene glycol or ethanol with the claimed components A and B. Instant disclosure states that the composition contains an additional hydrophilic phase contains polyethylene glycol and/or at least one lower alkanol selected from ethanol and propylene glycol (lines bridging page 1-2). However, there is no support for a composition consisting of the claimed components alone. Further, on page 2, it is disclosed that compositions may contain polyethylene glycol, which may be a part of the surfactant 15 for example if this is produced by polyethoxylation or added separately, from e.g. 1 to 40% of the formulation. Thus, it is evident from the disclosure that applicants did not conceive a composition that consists of only the claimed elements that includes a combination of PEG with a lower alkanol. Further, applicants have not envisioned a composition that excludes other components other than the claimed ones. For instance, instant specification supports the inclusion of poloxamer F68, which is a nonionic surfactant, which applicants argue that the instant claims do not allow (see applicants' arguments dated 4-21-09, page 4, paragraph 1).



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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lakshmi S. Channavajjala whose telephone number is 571-272-0591. The examiner can normally be reached on 9.00 AM -5.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila G. Landau can be reached on 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lakshmi S Channavajjala/  
Primary Examiner, Art Unit 1611  
July 3, 2009